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=> s l1 (A) (free or unbound)
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TI Improved method for diagnosing acute coronary syndrome
IN Qin, Qiu-Ping; Pettersson, Kim
PA Finland
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
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WO 2005073727	A1	20050811	WO 2005-FI36	20050119

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2004-539431P P 20040128

AB This invention concerns a bioaffinity assay for quant. determination in a sample of **free PAPP-A**, defined as the pregnancy associated plasma protein A (PAPP-A) that is not complexed to the proform of major basic protein (proMBP), wherein **free PAPP-A** is determined either (i) as a calculated difference between measured total PAPP-A and measured PAPP-A complexed to proMBP, or (ii) by a direct

bioaffinity assay measuring only **free PAPP-A**
. Furthermore, the invention concerns a method for diagnosing an acute
coronary syndrome in a person by using as marker either **free PAPP-A** as such or a ratio **free PAPP-A**/total **PAPP-A**, **free PAPP-A**/PAPP-A complexed to proMBP, or PAPP-A complexed to proMBP/total PAPP-A.
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L4 ANSWER 2 OF 31 MEDLINE on STN DUPLICATE 1
AN 2005275040 MEDLINE
DN PubMed ID: 15906426
TI Ethnicity and the need for correction of biochemical and ultrasound
markers of chromosomal anomalies in the first trimester: a study of
Oriental, Asian and Afro-Caribbean populations.
AU Spencer K; Heath V; El-Sheikhah A; Ong C Y T; Nicolaides K H
CS Prenatal Screening Unit, Clinical Biochemistry Department, Harold Wood
Hospital, Essex, UK.. KevinSpencer1@aol.com
SO Prenatal diagnosis, (2005 May) 25 (5) 365-9.
Journal code: 8106540. ISSN: 0197-3851.
CY England: United Kingdom
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 20050527
Last Updated on STN: 20050911
Entered Medline: 20050909
AB OBJECTIVES: To assess whether there is a need to correct first-trimester
biochemical markers (free beta-hCG and pregnancy-associated plasma
protein-A (PAPP-A)) or first-trimester fetal nuchal translucency thickness
(NT) in different ethnic groups, when screening for Downs syndrome at
11-14 weeks of gestation. METHODS: Free beta-hCG, PAPP-A and fetal NT
were measured at 11-14 weeks of gestation in a group of women presenting
for first-trimester screening in two OSCAR centres. The group comprised
61 219 sets of data from Caucasian women (the reference group); 4835 sets
of data from South Asian women; 3450 sets of data from Oriental women and

2727 sets of data from Afro-Caribbean women. The Oriental data set was supplemented with a further 480 cases collected in Hong Kong and the Afro-Caribbean data set was supplemented with 216 cases collected from Kings College. The difference in marker values between the reference group and the other ethnic groups was compared before and after weight correction for the biochemical markers using standard statistical techniques. A correction factor for ethnic origin was applied for all three markers and the screen-positive rate before and after correction was assessed for the various groups. RESULTS: After maternal weight correction, in Afro-Caribbean women, the median PAPP-A was increased by 55% and the free beta-hCG increased by 11%. In south Asian women, the PAPP-A was increased by 8% and the free beta-hCG decreased by 7.5%. In Oriental women, the PAPP-A was increased by 9% and the free beta-hCG by 6%. For delta NT in Afro-Caribbean women, the values were 0.064 mm lower on average than in Caucasian women and for south Asian women 0.045 mm lower. The difference of -0.012 for Oriental women was not significant. Before correcting for ethnic origin, these changes resulted in the screen-positive rates being lower in the Afro-Caribbean group (3.7% vs 5.6%), the south Asian group (4.3% vs 5.6%) and Oriental group (4.9% vs 5.6%). After correction, the screen-positive rates were largely similar in the four groups. CONCLUSION: Differences in median **PAPP-A**, **free** beta-hCG and, to a lesser extent, in NT exist in Afro-Caribbean, South Asian and Oriental women. In populations where the medians and delta NT reference ranges are established in predominantly Caucasian populations, some correction for ethnicity is appropriate and can redress differences in screen-positive rates between these different groups.

L4 ANSWER 3 OF 31 MEDLINE on STN DUPLICATE 2

AN 2005439558 IN-PROCESS
DN PubMed ID: 16104674
TI First trimester screening: the BUN study.
AU Wapner Ronald J
CS Department of Obstetrics and Gynecology, Drexel University College of
Medicine, Philadelphia, PA 19102, USA.. rw2191@columbia.edu
NC HD32109 (NICHD)
R01 HD31991 (NICHD)
SO Seminars in perinatology, (2005 Aug) 29 (4) 236-9.
Journal code: 7801132. ISSN: 0146-0005.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20050818
Last Updated on STN: 20050923
AB First trimester risk assessment for trisomies 21 and 18 is rapidly
transitioning from an investigational procedure performed at a few major
centers to the clinical arena. The BUN study (Biochemistry, Ultrasound,
Nuchal translucency) was conceived to evaluate the performance of first
trimester screening using **PAPP-A**, **free** beta
HCG, and ultrasound measurement of the nuchal translucency when introduced
into practice. Over a 4-year period, 13 prenatal diagnostic centers
evaluated over 8500 patients and reported an 85.2% trisomy 21 detection
rate with a 9.4% false positive rate. Further evaluation of the data
revealed that, once training and experience were accomplished,
sonographers could perform NT measurements consistent with reported
standards. In approximately half of the patients enrolled in the study,
second trimester serum analytes were obtained leading to additional
trisomy 21 detection but with an unacceptably high false positive rate. A
"sequential contingency" screening approach using both first and second
trimester values in some patients may provide the additional detection
afforded by measuring second trimester analytes with a limited invasive
procedure rate.

L4 ANSWER 4 OF 31 MEDLINE on STN DUPLICATE 3

AN 2005119989 MEDLINE
DN PubMed ID: 15712330
TI Re-evaluation of risk for Down syndrome by means of the combined test in
pregnant women of 35 years or more.
AU Centini Giovanni; Rosignoli Lucia; Scarinci Renato; Faldini Elisa; Morra
Carmina; Centini Gabriele; Petraglia Felice
CS Prenatal Diagnosis Centre, Chair of Obstetrics and Gynecology, Department
of Pediatrics, Obstetrics, and Reproductive Medicine, University of Siena,
Siena Italy.. centini@unisi.it
SO Prenatal diagnosis, (2005 Feb) 25 (2) 133-6.
Journal code: 8106540. ISSN: 0197-3851.
CY England: United Kingdom
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200506
ED Entered STN: 20050308
Last Updated on STN: 20050610
Entered Medline: 20050609
AB OBJECTIVE: Evaluation of combined test in pregnant women 35 years of age
and over to detect fetal Down syndrome. MATERIALS AND METHODS: The study
population included 408 pregnant women of 35 years and over, who requested
the combined test (nuchal translucency, **PAPP-A**,
free beta hCG, maternal age, cut-off 1:250) before deciding
whether to undergo amniocentesis. RESULTS: The test was positive in 66
women who then requested amniocentesis for fetal karyotype determination;
the other women had a negative test and declined amniocentesis.
False-positives increased with maternal age from 6.6% at 35 years to about
50% at 40 to 41 and 100% in women over 41. Six cases of Down syndrome and
two cases of trisomy 18 were detected. Not a single case of Down syndrome
or trisomy 18 was missed, and other chromosome abnormalities were detected
as well. CONCLUSIONS: The application of the combined test reduced the
need for invasive testing to only 14% of the studied pregnant population,
without missing any of the fetuses with trisomy 21 or 18.

L4 ANSWER 5 OF 31 MEDLINE on STN DUPLICATE 4
AN 2005305897 MEDLINE
DN PubMed ID: 15952984
TI Inhibin A is a maternal serum marker for Down's syndrome early in the
first trimester.
AU Christiansen M; Norgaard-Pedersen B
CS Department of Clinical Biochemistry, Statens Serum Institut, Copenhagen,
Denmark.. mic@ssi.dk
SO Clinical genetics, (2005 Jul) 68 (1) 35-9.
Journal code: 0253664. ISSN: 0009-9163.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200509
ED Entered STN: 20050615
Last Updated on STN: 20050922
Entered Medline: 20050921
AB Inhibin A is a maternal serum marker for fetal Down's syndrome (DS) in the
second trimester. We examined whether inhibin A could be used early in
the first trimester. Maternal serum concentrations of inhibin A were
determined in 81 controls and 27 cases of fetal trisomy 21 in gestational
week 5-11. The log MoM (Multiple of the Median of normal pregnancies)
inhibin A concentration in DS pregnancies increased with gestational age
(p = 0.001) from a mean log MoM (standard deviation) of -0.1754 (0.3712)
(n = 11) in week 7-8 to a mean log MoM (standard deviation) of 0.1842
(0.2145) (n = 12) in week 9-11. This corresponded to an increase in
inhibin median MoM from 0.67 to 1.53. When inhibin A was used together
with **pregnancy-associated plasma**
protein-A, free beta-human chorionic
gonadotrophin and nuchal translucency as DS markers, the estimated
detection rates were 81.4 and 82.6% in weeks 7-8 and 9-11, respectively,
for false-positive rates of 0.9 and 1.0%. The performance of the latter
combination early in the first trimester is nearly as good as that of
integrated first- and second-trimester screening, with the further

advantage that the risk can be reported to the pregnant woman in first trimester.

L4 ANSWER 6 OF 31 MEDLINE on STN DUPLICATE 5
AN 2004535898 MEDLINE
DN PubMed ID: 15507981
TI First-trimester maternal serum PAPP-A and free-beta subunit human chorionic gonadotropin concentrations and nuchal translucency are associated with obstetric complications: a population-based screening study (the FASTER Trial).
AU Dugoff Lorraine; Hobbins John C; Malone Fergal D; Porter T Flint; Luthy David; Comstock Christine H; Hankins Gary; Berkowitz Richard L; Merkatz Irwin; Craigo Sabrina D; Timor-Tritsch Ilan E; Carr Steven R; Wolfe Honor M; Vidaver John; D'Alton Mary E
CS Department of Gynecology and Obstetrics, University of Colorado Health Sciences Center, Denver, CO, USA.
NC R01 HD 38652 (NICHD)
SO American journal of obstetrics and gynecology, (2004 Oct) 191 (4) 1446-51.
Journal code: 0370476. ISSN: 0002-9378.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200412
ED Entered STN: 20041028
Last Updated on STN: 20041220
Entered Medline: 20041207
AB OBJECTIVE: The purpose of this study was to determine whether maternal serum levels of **pregnancy-associated plasma protein A**, **free**-beta subunit human chorionic gonadotropin, or nuchal translucency size are associated with obstetric complications. STUDY DESIGN: Data were obtained from the First and Second Trimester Evaluation of Risk trial. Pregnancy-associated plasma protein A and free-beta subunit human chorionic gonadotropin levels were analyzed, and nuchal translucency was measured between 10 weeks 3 days and 13 weeks 6 days of gestation in 34,271 pregnancies. RESULTS: Women with pregnancy-associated plasma protein A of < or =5th percentile were significantly more likely to experience spontaneous fetal loss at < or =24

weeks of gestation, low birth weight, preeclampsia, gestational hypertension, preterm birth (P < .001) and stillbirth, preterm premature rupture of membranes, and placental abruption (P < .02). Nuchal translucency at > or =99th percentile and free-beta subunit human chorionic gonadotropin at < or =1st percentile were associated with an increased risk of spontaneous loss at < or =24 weeks of gestation (adjusted odds ratios, 3.90, 3.62, respectively; P < .001). CONCLUSION: Low pregnancy-associated plasma protein A levels in the first trimester were associated strongly with a number of adverse pregnancy outcomes. Low free-beta subunit human chorionic gonadotropin levels and large nuchal translucency were both associated with early fetal loss.

L4 ANSWER 7 OF 31 MEDLINE on STN DUPLICATE 6
AN 2004502014 MEDLINE
DN PubMed ID: 15459938
TI Audit on nuchal translucency thickness measurements in Flanders, Belgium: a plea for methodological standardization.
AU Gyselaers W J A; Vereecken A J; Van Herck E J H; Straetmans D P L; de Jonge E T M; Ombelet W U A M; Nijhuis J G
CS Department of Obstetrics and Gynaecology, Ziekenhuis Oost Limburg, Genk, Belgium.. wilfried.gyselaers@zol.be
SO Ultrasound in obstetrics & gynecology : official journal of the International Society of Ultrasound in Obstetrics and Gynecology, (2004 Oct) 24 (5) 511-5.
Journal code: 9108340. ISSN: 0960-7692.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200504
ED Entered STN: 20041008
Last Updated on STN: 20050412
Entered Medline: 20050411
AB OBJECTIVES: To audit nuchal translucency thickness (NT) measurements for fetal aneuploidy screening in Flanders, and to estimate the impact of small variations in NT measurement on the screening result of two first-trimester screening algorithms: maternal age + NT (Algorithm A), and maternal age + NT + **pregnancy associated plasma protein-A** + **free** beta-human

chorionic gonadotropin (Algorithm B). METHODS: We used the database of first-trimester combined screening, as collected by the General Medical Laboratory AML in Antwerp, Belgium, between 1 January 2001 and 1 April 2004. Audit was performed by establishing a delta-NT distribution curve for one trainee of The Fetal Medicine Foundation (FMF) and for a group of 263 other sonographers, in comparison with the FMF reference values. Risks for fetal aneuploidy were calculated at a cut-off value of 1 : 300 for Algorithm A and 1 : 150 for Algorithm B. These risks were recalculated in both algorithms after a modeled increase of all NT values by 0.1 or 0.2 mm. RESULTS: In a total of 592 measurements performed by the FMF trainee, the 5th, 50th and 95th percentiles of delta-NT measurements were at -0.41, +0.03 and +0.68 mm, respectively. These values were close to the FMF reference values. The screen-positive rate for this set of data was 4.4% (26/592) in both algorithms. For the 12 555 measurements of the 263 other sonographers, the 5th, 50th and 95th percentiles of delta-NT were at -0.81, -0.14 and +0.73 mm, respectively, which clearly indicates underestimation of NT in the lower range. In this set of data the screen-positive rate was 3.5% for both algorithms (439/12 555 for Algorithm A and 436/12 555 for Algorithm B). Also in this group, 5% (59/1186) of negative screening results at maternal age > or = 35 years in Algorithm A became positive after a modeled 0.1-mm increase in NT, whereas this was only in 1.2% (134/11 369) of tests at maternal age < 35 years ($P < 0.0001$). The overall increase of screen-positive rate in Algorithm A after an NT modification of +0.1 mm was 1.2% (152/12 555), significantly more than in Algorithm B (86/12 555; 0.7%) ($P < 0.0001$). CONCLUSION: In Flanders, there is a systematic underestimation of NT in comparison with the FMF reference range. Attempts to change these

measurements according to the FMF criteria are crucial. This will mainly influence the screening results of women at advanced maternal age and of NT-based algorithms without the use of other parameters.

L4 ANSWER 8 OF 31 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
AN 2004265280 EMBASE
TI [Smoking in pregnancy. Influence on **pregnancy-associated plasma protein A**, **free** β-hCG and nuchal transparency].
RAUCHEN IN DER SCHWANGERSCHAFT. EINFLUSS AUF SCHWANGERSCHAFTSASSOZIIERTES PLASMAPROTEIN A, FREIES β-HCG UND NACKENTRANSPARENZ.
AU Geipel A.; Gembruch U.
CS Dr. A. Geipel, Abt. Geburtshilfe/Pranatale Med., Zentrum Geburtshilfe/Frauenheilkunde, Universitatsklinikum, Sigmund-Freud-Strasse 25, 53105 Bonn, Germany. annegeipel@hotmail.com
SO Gynakologe, (2004) Vol. 37, No. 5, pp. 473-474.
Refs: 9
ISSN: 0017-5994 CODEN: GYNKAP
CY Germany
DT Journal; General Review
FS 010 Obstetrics and Gynecology
014 Radiology
017 Public Health, Social Medicine and Epidemiology
LA German
ED Entered STN: 20040709
Last Updated on STN: 20040709

L4 ANSWER 9 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2005:276474 BIOSIS
DN PREV200510063648
TI The effect of vaginal bleeding on maternal serum **PAPP-A**, **free** beta-hCG, and nuchal translucency. A population based screening study (the faster trial).
AU Dugoff, Lorraine [Reprint Author]; Faber, Vincent; Hobbins, John; Malone, Fergal; Canick, Jacob; Porter, Flint; Luthy, David; Comstock, Christine; Bukowski, Radek; Eddleman, Keith; Gross, Susan; Craigo, Sabrina; Timor-Trisch, Ilan; Carr, Stephen; Wolfe, Honor; D'Alton, Mary E.
CS Univ Colorado, Hlth Sci Ctr, Denver, CO USA
SO American Journal of Obstetrics and Gynecology, (DEC 2004) Vol. 191, No. 6, pp. S47.
Meeting Info.: 25th Annual Meeting of the Society-for-Maternal-Fetal-

Medicine. Reno, NV, USA. February 09 -12, 2005. Soc Maternal Fetal Med.
CODEN: AJOGAH. ISSN: 0002-9378.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jul 2005
Last Updated on STN: 27 Jul 2005

L4 ANSWER 10 OF 31 MEDLINE on STN DUPLICATE 7
AN 2004354404 MEDLINE
DN PubMed ID: 15228997
TI **Pregnancy-associated plasma protein A, free** beta-hCG, nuchal translucency, and risk of pregnancy loss.
AU Goetzl Laura; Krantz David; Simpson Joe Leigh; Silver Richard K; Zachary Julia M; Pergament Eugene; Platt Lawrence D; Mahoney Maurice J; Wapner Ronald J
CS Baylor College of Medicine, Houston, Texas, USA.. lgoetzl@bcm.tmc.edu
NC HD32109 (NICHD)
R01 HD31991 (NICHD)
SO Obstetrics and gynecology, (2004 Jul) 104 (1) 30-6.
Journal code: 0401101. ISSN: 0029-7844.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200407
ED Entered STN: 20040720
Last Updated on STN: 20040801
Entered Medline: 20040730
AB OBJECTIVE: To estimate the likelihood of clinical early and late pregnancy loss as a function of first-trimester maternal serum analytes and fetal nuchal translucency measurements. METHODS: Study subjects were recruited for a National Institute of Child Health and Human Development-sponsored multicenter cohort study initially designed to study the detection of Down syndrome during the first trimester of pregnancy. The cohort consisted of women who had a live fetus between 10 and 14 weeks of gestation and had no significant vaginal bleeding. Women with prior fetal trisomy (T21/18) and those with structural or chromosomal abnormalities in the index pregnancy

were excluded. First-trimester screening consisted of pregnancy-associated plasma protein A (**PAPP-A**), **free** beta-hCG, and nuchal translucency. Pregnancy loss rates in women with various levels of **PAPP-A**, **free** beta-hCG, or nuchal translucency (less than 1st, less than 5th, more than 95th, and more than 99th percentile) were compared with losses in women with normal values (5th to 95th percentile). RESULTS: The mean gestational age at screening of 7,932 women meeting study criteria was 12.1 weeks. Loss rates were only 0.36% at less than 20 weeks after normal free beta-hCG, PAPP-A, and nuchal translucency. Conversely, low levels of PAPP-A and free beta-hCG as well as increased nuchal translucency were individually associated with increased early loss. These associations persisted after controlling for maternal age and race using logistic regression analysis. CONCLUSION: Normal values of **PAPP-A**, **free** beta-hCG, and nuchal translucency are associated with a very low risk of pregnancy loss at less than 20 weeks.

L4 ANSWER 11 OF 31 MEDLINE on STN DUPLICATE 8
AN 2003313785 MEDLINE
DN PubMed ID: 12842057
TI The influence of smoking on the **pregnancy-associated plasma protein A**, **free** beta human chorionic gonadotrophin and nuchal translucency.
AU Niemimaa Marko; Heinonen Seppo; Seppala Maija; Ryynanen Markku
CS Department of Obstetrics and Gynaecology, Oulu University Hospital, Finland.
SO BJOG : an international journal of obstetrics and gynaecology, (2003 Jul) 110 (7) 664-7.
Journal code: 100935741. ISSN: 1470-0328.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 200308
ED Entered STN: 20030708
Last Updated on STN: 20030820
Entered Medline: 20030819
AB OBJECTIVE: To analyse the effects of smoking on first trimester parameters used in prenatal screening for Down's Syndrome. DESIGN: A chart study. SETTING: Primary care centres and maternity clinics of the participating

universities' and central hospitals. POPULATION: Three thousand and one hundred fifteen women screened by nuchal translucency measurement and 4436 women screened by maternal serum samples. Only normal singleton pregnancies were included. METHODS: The mean multiples of median of pregnancy associated plasma protein A (**PAPP-A**), **free** beta human chorionic gonadotrophin (beta-hCG) and nuchal translucency were compared by independent samples t test after logarithmic transformation of the data between smokers and non-smokers. MAIN OUTCOME MEASURES: PAPP-A and free beta-hCG concentrations and nuchal translucency measurements. RESULTS: PAPP-A was significantly reduced and nuchal translucency increased if the mother smoked. The smokers were more frequently considered as being at high risk for Down's Syndrome. CONCLUSIONS: Correcting PAPP-A median for smokers down by 20% might improve the accuracy of the risk evaluations given to individual women. If the association between increased nuchal translucency and smoking can be confirmed, it poses interesting questions as to the reasons for increased nuchal translucency among normal pregnancies.

L4 ANSWER 12 OF 31 MEDLINE on STN DUPLICATE 9
AN 2003286062 MEDLINE
DN PubMed ID: 12813760
TI Early vaginal bleeding and first-trimester markers for Down syndrome.
AU De Biasio Pierangela; Canini Silvana; Crovo Angela; Prefumo Federico; Venturini Pier Luigi
CS UO di Ostetricia e Ginecologia, Istituto "G Gaslini", Universita di Genova, Italy.. bnhdeb@libero.it
SO Prenatal diagnosis, (2003 Jun) 23 (6) 470-3.
Journal code: 8106540. ISSN: 0197-3851.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20030619
Last Updated on STN: 20031017
Entered Medline: 20031016
AB OBJECTIVES: To assess the effect of early vaginal bleeding on

first-trimester markers for Down syndrome. METHODS: A retrospective study was conducted on 2330 normal singleton fetuses who underwent first-trimester combined screening for Down syndrome based on ultrasound and maternal serum markers. Fetal nuchal translucency (NT), maternal serum pregnancy-associated plasma protein A (**PAPP-A**), **free** beta-hCG and the false-positive rate of the test were compared between pregnancies with (n = 253) and without (n = 2077) a history of early vaginal bleeding. RESULTS: The mean +/- SD log(10) MoM for NT, PAPP-A and free beta-hCG was -0.024 +/- 0.101, 0.007 +/- 0.244, 0.047 +/- 0.273 and -0.011 +/- 0.108, -0.006 +/- 0.223, 0.008 +/- 0.264 in pregnancies with and without a history of early vaginal bleeding, with a p value of 0.07, 0.40 and 0.03 respectively. The false-positive rate was 2.4% and 3.6% (p = 0.33). CONCLUSIONS: An earlier episode of vaginal bleeding is associated with an increase in maternal serum free beta-hCG levels at first-trimester combined screening for Down syndrome. However, this phenomenon is unlikely to significantly affect the false-positive rate of the test.

L4 ANSWER 13 OF 31 EMBASE

AN 2003245273 EMBASE

TI First and second trimester antenatal screening for Down's syndrome: The results of the Serum, Urine and Ultrasound Screening Study (SURUSS).

AU Wald N.J.; Rodeck C.; Hackshaw A.K.; Walters J.; Chitty L.; Mackinson A.M.

CS Prof. N.J. Wald, Dept. of Environ./Prev. Medicine, Wolfson Inst. of Preventive Medicine, Bart's/the London Sch. of Med./Dent., London, EC1M 6BQ, United Kingdom. n.j.wald@qmul.ac.uk

SO Journal of Medical Screening, (2003) Vol. 10, No. 2, pp. 56-104. Refs: 50
ISSN: 0969-1413 CODEN: JMSCFE

CY United Kingdom

DT Journal; Article

FS 010 Obstetrics and Gynecology
017 Public Health, Social Medicine and Epidemiology
LA English
SL English
ED Entered STN: 20030710
Last Updated on STN: 20030710
AB Objectives: To identify the most effective, safe and cost-effective method of antenatal screening for Down's syndrome using nuchal translucency (NT), maternal serum and urine markers in the first and second trimesters of pregnancy, and maternal age in various combinations. Design: A prospective study of women who booked for their antenatal care at about 8-14 weeks of gestation, with follow-up to identify pregnancies with Down's syndrome ascertained through second trimester screening or at birth. Setting: Twenty-five maternity units (24 in the UK and one in Austria) offering second trimester Down's syndrome serum screening that agreed to collect observational data in the first trimester. Participants: The results were based on 47,053 singleton pregnancies, including 101 pregnancies with Down's syndrome. Measurements and tests: NT measurements were included if obtained between 9 and 13 weeks of pregnancy; serum and urine samples were also taken and stored. Another pair of serum and urine samples was collected in the second trimester and included if obtained between 14 and 20 weeks. Urine and serum samples from each affected pregnancy and five matched controls were tested for: Serum: alphafetoprotein (AFP) total human chorionic gonadotrophin (hCG) unconjugated oestriol (uE(3)) pregnancy associated plasma protein A (**PAPP-A**) **free** β-hCG dimeric inhibin-A. Urine: invasive trophoblast antigen (ITA) β-core fragment total hCG free β-hCG. The matching criteria were gestation (using an ultrasound crown-rump length or biparietal diameter measurement), duration of storage, and centre. Screening performance of the individual markers and combinations of markers together with maternal age was assessed using

standard methods. In addition pairs of first and second trimester serum samples from 600 controls were tested to secure a larger set in which screening performance could be determined using distribution parameters based on dates (time since first day of the last menstrual period). Main outcome measures: The following were determined for different combinations of markers: efficacy (by assessing screening performance, focusing on the false-positive rate (FPR) for an 85% detection rate (DR)) safety (focusing on the number of fetal losses due to amniocentesis (or chorionic villus sampling) in 100,000 women screened) cost-effectiveness (focusing on the cost of screening 100,000 women and the cost per Down's syndrome pregnancy diagnosed). Results: Efficacy (screening performance): The false-positive rates for an 85% detection rate for the main screening tests are shown in the above table, in decreasing order of screening performance: With the serum integrated test, 10 weeks is the preferred time in pregnancy for the PAPP-A measurement. For the integrated test and the combined test, the timing of the measurement of the first trimester markers is less critical. Safety: The lower false-positive rate with the integrated test compared with other tests means that at an 85% detection rate there would be nine diagnostic procedure-related unaffected fetal losses per 100,000 women screened compared with 44 using the combined test or 45 with the quadruple test. Cost-effectiveness: Screening using the integrated test is less costly than might be expected because the extra screening costs tend to be offset by savings in the cost of diagnosis arising from the low false-positive rate. It was estimated that to achieve an 85% detection rate the cost to the UK NHS would be £15,300 per Down's syndrome pregnancy detected. The corresponding cost using the second trimester quadruple test would be £16,800 and using the first trimester combined

test it would be £19,000. Conclusions: Implications for healthcare:
The results showed that screening performance in the first trimester of
pregnancy was virtually the same as that in the second trimester, and in
either it was much less effective than integrating screening measurements
from both trimesters into a single test. In applying these results to
screening practice several conclusions can be drawn. The following tests
offer the most effective and safe method of screening: overall: the
integrated test if an NT measurement is not available: the serum
integrated test for women who do not attend for antenatal care until the
second trimester of pregnancy: the quadruple test for women who choose to
have a screening test in the first trimester: the combined test. At a
constant detection rate, the cost-effectiveness of these four tests is
broadly similar, any extra screening costs tending to be offset by fewer
diagnostic costs. The evidence presented in this report does not support
retaining the double test, the triple test, or NT measurements on their
own (with or without maternal age) because each would lead to many more
women having invasive diagnostic tests, without increasing the proportion
of Down's syndrome pregnancies detected.

L4 ANSWER 14 OF 31 MEDLINE on STN DUPLICATE 10
AN 2001512240 MEDLINE
DN PubMed ID: 11559909
TI Assessment of the value of reporting partial screening results in prenatal
screening for Down syndrome.
CM Comment in: Prenat Diagn. 2002 Jul;22(7):633; author reply 633-4. PubMed
ID: 12124702
AU Hackshaw A K; Wald N J
CS Department of Environmental and Preventive Medicine, Wolfson Institute of
Preventive Medicine, Queen Mary and Westfield College, University of
London, London, UK.. a.k.hackshaw@mds.qmw.ac.uk
SO Prenatal diagnosis, (2001 Sep) 21 (9) 737-40.
Journal code: 8106540. ISSN: 0197-3851.

CY England: United Kingdom
DT (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200111
ED Entered STN: 20010918
Last Updated on STN: 20030125
Entered Medline: 20011101
AB Prenatal screening for Down syndrome can be performed using the first trimester Combined Test [nuchal translucency (NT), pregnancy-associated plasma protein A (**PAPP-A**), **free** beta-human chorionic gonadotrophin (hCG) and maternal age] or the Integrated Test (for example, NT and PAPP-A in the first trimester and two or more serum markers in the second trimester, all with maternal age). We investigated the value of providing partial results when using the Combined Test or Integrated Test to identify women with a high enough risk of having an affected pregnancy based on NT and maternal age alone such that there would be little advantage in combining this information with data on the serum markers. We also assessed whether in programmes using the Integrated Test it is worthwhile reporting partial results based on risk using first trimester markers and not obtaining a second trimester blood sample. Published data based on 480 affected and 96 839 unaffected pregnancies were used for the present study. Using NT and age alone, about 0.14% of all women screened would have such a high risk that they would always remain screen-positive after the Combined Test and only 0.06% would remain screen-positive after the Integrated Test. Similarly, about 0.07% of all women screened who have a high risk based on NT, PAPP-A and age would remain screen-positive after the Integrated Test. These percentages are too small to justify reporting two risk estimates for all women, given the confusion this would generate. It is therefore not worthwhile reporting partial risk estimates in screening programmes using

the Combined Test or Integrated Test.
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L4 ANSWER 15 OF 31 MEDLINE on STN DUPLICATE 11
AN 2001387113 MEDLINE
DN PubMed ID: 11440550
TI Three-dimensional ultrasound measurement of the placental volume in early
pregnancy: method and correlation with biochemical placenta parameters.
AU Metzenbauer M; Hafner E; Hoefinger D; Schuchter K; Stangl G; Ogris E;
Philipp K
CS Ludwig-Boltzmann-Institute of Clinical Obstetrics and Gynaecology,
Donauspital am SMZ-Ost, Langobardenstrasse 122, A-1220 Vienna, Austria..
martin.metzenbauer@smz.magwien.gv.at
SO Placenta, (2001 Jul) 22 (6) 602-5.
Journal code: 8006349. ISSN: 0143-4004.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200109
ED Entered STN: 20011001
Last Updated on STN: 20021030
Entered Medline: 20010927
AB Placental size has been an interesting topic of research for many years.
The main aim of this study was to investigate the feasibility of measuring
the placental volume at the end of the first trimester using
three-dimensional (3D) ultrasound and to correlate these volumes to known
placental functional indices and to factors affecting the placenta. Women
with singleton pregnancies at the end of the first trimester were included
into this study. The volume data of the placentae were correlated to the
crown-rump length (CRL), placenta-associated plasma protein A (**PAPP-A**), **free** beta-human chroangiogonadotropin
(f-beta-hCG) and other factors that may affect the placental size or
function. A total of 1462 pregnancies could be evaluated. Comparison
between CRL and placental volume proved a significant correlation (r=0.43,
P< 0.001). Due to the observed proportional growth of CRL and placental
volume, a quotient (placental volume/CRL) was calculated for each case.

There were no differences between placenta/CRL-quotients in relation to gravidity, parity or smoking. Correlations could be established between the placental volume and PAPP-A and f-beta-hCG (PAPP-A: r=0.28, P< 0.001, f-beta-hCG: r=0.10, P< 0.001). The measurement of the placenta in the first trimester can be performed in a high percentage of cases. The placenta/CRL quotient represents a simple method to compare placentae from different gestational days. The correlation between placental volume and maternal serum screening parameters might provide a chance to refine first trimester Down's syndrome serum screening. Future studies will be needed to evaluate the possible clinical use of first trimester placental volume measurements.

L4 ANSWER 16 OF 31 MEDLINE on STN DUPLICATE 12
AN 2001446864 MEDLINE
DN PubMed ID: 11494292
TI First trimester screening for Down syndrome and assisted reproduction: no basis for concern.
AU Wojdemann K R; Larsen S O; Shalmi A; Sundberg K; Christiansen M; Tabor A
CS Department of Obstetrics and Gynaecology, Hvidovre Hospital, Copenhagen University, Copenhagen, Denmark.
SO Prenatal diagnosis, (2001 Jul) 21 (7) 563-5.
Journal code: 8106540. ISSN: 0197-3851.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20010813
Last Updated on STN: 20011008
Entered Medline: 20011004
AB In pregnancies obtained after assisted reproduction the false-positive rate of second trimester Down syndrome (DS) screening is increased by 1.5-3-fold. This may cause an increase in the number of amniocenteses and the fetal loss rate. The present study for the first time examined

whether assisted reproductive technologies affect the results of first trimester screening. The markers **PAPP-A**, **free** beta-hCG and the nuchal translucency (NT) thickness were examined at 12-14 weeks' gestation. Screening markers in 47 in vitro fertilisation (IVF), 63 ovulation induction (OI) and 3026 spontaneously conceived singleton pregnancies were compared. The MoM (multiples of the median) value in the IVF pregnancies was 1.02 (95% CI: 0.85-1.22) for PAPP-A, 1.14 (95% CI: 0.95-1.37) for beta-hCG and 0.97 (95% CI: 0.89-1.05) for NT; the MoM value in the OI pregnancies was 0.89 (95% CI: 0.76-1.05) for PAPP-A, 1.08 (95% CI: 0.93-1.25) for beta-hCG and 1.02 (95% CI: 0.95-1.11) for NT. The first trimester marker values in assisted reproductive pregnancies and spontaneously conceived pregnancies were not significantly different. Estimated false-positive rates for a risk cut-off of 1:400 varied from 4.7% in IVF pregnancies to 5.1% in OI pregnancies. Therefore the false-positive rate in Down syndrome screening should be independent of the method of conception.

L4 ANSWER 17 OF 31 MEDLINE on STN DUPLICATE 13
AN 2001446861 MEDLINE
DN PubMed ID: 11494288
TI First trimester PAPP-A in the detection of non-Down syndrome aneuploidy.
AU Ochshorn Y; Kupferminc M J; Wolman I; Orr-Urtreger A; Jaffa A J; Yaron Y
CS Prenatal Diagnosis Unit, Genetic Institute, Sourasky Medical Center, 6 Weizmann Street, Tel Aviv 64239, Israel.
SO Prenatal diagnosis, (2001 Jul) 21 (7) 547-9.
Journal code: 8106540. ISSN: 0197-3851.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20010813
Last Updated on STN: 20011008
Entered Medline: 20011004
AB Combined first trimester screening using pregnancy associated plasma

protein-A (**PAPP-A**), **free** beta-human chorionic gonadotrophin, and nuchal translucency (NT), is currently accepted as probably the best combination for the detection of Down syndrome (DS). Current first trimester algorithms provide computed risks only for DS. However, low PAPP-A is also associated with other chromosome anomalies such as trisomy 13, 18, and sex chromosome aneuploidy. Thus, using currently available algorithms, some chromosome anomalies may not be detected. The purpose of the present study was to establish a low-end cut-off value for PAPP-A that would increase the detection rates for non-DS chromosome anomalies. The study included 1408 patients who underwent combined first trimester screening. To determine a low-end cut-off value for PAPP-A, a Receiver-Operator Characteristic (ROC) curve analysis was performed. In the entire study group there were 18 cases of chromosome anomalies (trisomy 21, 13, 18, sex chromosome anomalies), 14 of which were among screen-positive patients, a detection rate of 77.7% for all chromosome anomalies (95% CI: 55.7-99.7%). ROC curve analysis detected a statistically significant cut-off for PAPP-A at 0.25 MoM. If the definition of screen-positive were to also include patients with PAPP-A<0.25 MoM, the detection rate would increase to 88.8% for all chromosome anomalies (95% CI: 71.6-106%). This low cut-off value may be used until specific algorithms are implemented for non-Down syndrome aneuploidy.

L4 ANSWER 18 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2001:202868 BIOSIS

DN PREV200100202868

TI Combined biochemical and sonographic first-trimester screening for Down syndrome and other chromosome anomalies.

AU Yaron, Yuval [Reprint author]; Ochshorn, Yifat; Evans, Mark; Kupferminc,
Michael; Wolman, Igal; Orr-Urtreger, Avi; Jaffa, Ariel
CS Tel Aviv Sourasky Medical Center, Tel Aviv University, Genetic Institute,
Tel Aviv, Israel
SO American Journal of Obstetrics and Gynecology, (January, 2001) Vol. 184,
No. 1, pp. S110. print.
Meeting Info.: 21st Annual Meeting of the Society for Maternal-Fetal
Medicine. Reno, Nevada, USA. February 05-10, 2001. Society for
Maternal-Fetal Medicine.
CODEN: AJOGAH. ISSN: 0002-9378.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 25 Apr 2001
Last Updated on STN: 18 Feb 2002
AB OBJECTIVE: Combined screening using pregnancy-associated plasma protein-A
(**PAPP-A**), **free** beta-human chorionic
gonadotropin (Fbeta-hCG), and nuchal translucency (NT), is probably the
best combination for detection of Down syndrome (DS) in the first
trimester. Current algorithms provide computed risks only for DS, thus
some chromosome anomalies may not be detected. Low levels of PAPP-A are
associated with DS and other chromosomal anomalies. We have previously
shown a clinically significant low-end cutoff value for PAPP-A at 0.25
MoM. The purpose of this study was to evaluate a first-trimester
screening strategy that employs this cutoff in addition to the standard
algorithm. STUDY DESIGN: The study included 1408 patients with singleton
pregnancies who underwent combined first-trimester screening with NT,
PAPP-A and Fbeta-hCG at 10-13 weeks. Screen positive patients were
defined as those having a DS risk greater than 1 in 380 at birth or PAPP-A
lower than 0.25 MoM. These were given genetic counseling and offered
diagnostic testing by CVS or amniocentesis. RESULTS: A total of 116
patients were found to be screen positive, and 99 consented diagnostic
testing. In the entire study group, 18 patients had chromosomally

abnormal fetuses: 2 had DS, 4 had trisomy 18, 3 had trisomy 13, 8 had sex chromosome anomalies, and had chromosome 7q deletion. Using only the standard algorithm, 14 cases (78%) would have been detected. However, using the PAPP-A cutoff value as well, 16 (89%) of all chromosome anomalies were detected. CONCLUSIONS: Combined first-trimester screening using the standard algorithm and a PAPP-A cutoff < 0.25 MoM increased the detection rate for all chromosome anomalies.

L4 ANSWER 19 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2001:167447 BIOSIS
DN PREV200100167447
TI Prenatal screening strategies for Down syndrome.
AU Morris, T. Christopher [Reprint author]; Stringer, Jeffrey [Reprint author]; Biggio, Joseph, Jr.; Owen, John
CS OB/GYN, University of Alabama at Birmingham, Birmingham, AL, USA
SO American Journal of Obstetrics and Gynecology, (January, 2001) Vol. 184, No. 1, pp. S27. print.
Meeting Info.: 21st Annual Meeting of the Society for Maternal-Fetal Medicine. Reno, Nevada, USA. February 05-10, 2001. Society for Maternal-Fetal Medicine.
CODEN: AJOGAH. ISSN: 0002-9378.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Apr 2001
Last Updated on STN: 18 Feb 2002
AB OBJECTIVE: To evaluate the costs and effectiveness of 5 strategies for prenatal detection of Down syndrome (DS). STUDY DESIGN: A decision analysis model compared: (1) triple screen (TS): AFP, hCG, E3; (2) quad screen (QS): TS and inhibin A; (3) first-trimester (TM) screen (FIRST): **PAPP-A**, **free** beta-hCG, and nuchal translucency; (4) integrated screen (INT): FIRST + QS, but with no amniocentesis/CVS until QS results available; (5) sequential screen (SEQ): FIRST + QS, but with CVS option if FIRST abnormal. The hypothetical cohort consisted of 1 million women, age <35 years, and 1682 DS fetuses at

10 weeks' gestation. Estimates: lifetime cost of DS = dollar sign489,000;
amniocentesis/CVS uptake if screen positive = 70%; choose DS termination =
90%; amniocentesis loss = 0.8%; CVS loss = 1.2%; spontaneous DS loss from
10 to 15 weeks = 25%, 15 weeks to term = 23%. RESULTS: QS was least
expensive but had a cost-effectiveness of dollar sign515,000 per case
detected and dollar sign743,000 per DS live birth (LB) averted. SEQ cost
dollar sign18 more per patient than QS, but was far more cost-effective:
dollar sign275,000 per case detected. Sensitivity analysis considered
that first-trimester screening could lower second-trimester sensitivity
for SEQ and INT: SEQ remained preferable to other strategies if the
sensitivity of the second-trimester test remained >30%. CONCLUSIONS: If
first-trimester testing is unavailable, QS is superior to TS. The expense
of SEQ is clearly justified by its higher efficacy, even though it incurs
an incremental cost of dollar sign27,000 per case detected. In centers
offering first-trimester testing, the best strategy could depend on
patient preference for the lowest euploid loss rate (INT) versus the
highest detection rate (SEQ).

L4 ANSWER 20 OF 31 MEDLINE on STN DUPLICATE 14
AN 2000281773 MEDLINE
DN PubMed ID: 10820406
TI Maternal serum free beta-hCG and PAPP-A in fetal sex chromosome defects in
the first trimester.
AU Spencer K; Tul N; Nicolaides K H
CS Endocrine Unit, Clinical Biochemistry Department, Harold Wood Hospital,
Gubbins Lane, Romford, Essex RM3 0BE, UK..
Kevin_Spencer@Compuserve.com
SO Prenatal diagnosis, (2000 May) 20 (5) 390-4.
Journal code: 8106540. ISSN: 0197-3851.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200006

ED Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000630
AB We have studied maternal serum free beta-hCG and PAPP-A, and fetal nuchal
translucency (NT) in a series of 46 cases of fetal Turner's syndrome, 13
cases of other sex chromosomal anomalies and compared these with 947
control pregnancies in the first trimester. In cases of Turner's syndrome
(45,X) the median fetal NT was significantly higher than in controls (4.76
MoM), the median PAPP-A was significantly lower (0.49 MoM), whilst the
free beta-hCG was not significantly different (1.11 MoM). For NT, 93%
(43/46) of cases were equal to or greater than the 95th centile of
controls, for PAPP-A 35% (16/46) of cases were less than or equal to the
5th centile of controls and for free beta-hCG 15% (7/46) of cases were
equal to or greater than the 95th centile of controls. For other sex
chromosomal anomalies (47XXX, XXY, XYY) the median NT was increased (2.07
MoM) whilst PAPP-A was not significantly decreased (0.88 MoM) and free
beta-hCG was not significantly different (1.07 MoM) from controls. Using
a previously derived multivariate risk algorithm for trisomy 21,
incorporating NT, **PAPP-A**, **free** beta-hCG and
maternal age, 96% of the Turner's cases and 62% of the other sex
chromosomal anomalies would have been identified.

L4 ANSWER 21 OF 31 MEDLINE on STN DUPLICATE 15
AN 2001027029 MEDLINE
DN PubMed ID: 10986441
TI Biochemical screening for Down syndrome.
AU Cuckle H
CS Reproductive Epidemiology, Centre for Reproduction, Growth and
Development, School of Medicine, University of Leeds, 26 Clarendon Road,
LS2 9NZ, Leeds, UK.. h.s.cuckle@leeds.ac.uk
SO European journal of obstetrics, gynecology, and reproductive biology,
(2000 Sep) 92 (1) 97-101. Ref: 16
Journal code: 0375672. ISSN: 0301-2115.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200011
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001116
AB Maternal serum screening for Down syndrome is an established practise in many countries. In the second trimester human chorionic gonadotrophin (hCG) or free beta-hCG is the marker of first choice, with alpha-fetoprotein (AFP) as the second marker and unconjugated oestriol (uE(3)) the third. Statistical models with parameters derived by meta-analysis predict that a three marker combination will yield a 67% detection rate for a 5% false-positive rate. The model prediction have been confirmed in 21 large prospective intervention studies. A fourth marker, inhibin A, increases the detection rate by 7% for the same false-positive rate. In the first trimester, similar models predict that a combination of **pregnancy associated plasma protein A**, **free** beta-hCG, AFP and uE(3) will yield a 70% detection rate. This is increased to 88% if ultrasound nuchal translucency is used as an additional marker. Screening can also be extended to Edwards' syndrome, yielding high detection rates with little increase in the false-positive rate. Abnormal marker levels are also associated with a variety of adverse outcomes of pregnancy. High quality information and decision aids are needed to minimise anxiety among screenees.

L4 ANSWER 22 OF 31 MEDLINE on STN DUPLICATE 16
AN 1999382423 MEDLINE
DN PubMed ID: 10451512
TI Second-trimester pregnancy associated plasma protein-A levels are reduced in Cornelia de Lange syndrome pregnancies.
CM Comment in: Prenat Diagn. 2003 Oct;23(10):864. PubMed ID: 14558036
AU Aitken D A; Ireland M; Berry E; Crossley J A; Macri J N; Burn J; Connor J

M
CS Institute of Medical Genetics, Yorkhill, Glasgow G3 8SJ, U.K.. daitken@udcf.gla.ac.uk
SO Prenatal diagnosis, (1999 Aug) 19 (8) 706-10.
Journal code: 8106540. ISSN: 0197-3851.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA English
FS Priority Journals
EM 199911
ED Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991109
AB Maternal serum samples were collected from 19 pregnancies which resulted in the birth of a child with the classical Cornelia de Lange syndrome phenotype ascertained by careful clinical review. Using specific immunoassays, the serum levels of **pregnancy associated plasma protein-A**, **free**-beta human chorionic gonadotrophin and inhibin A were investigated. Pregnancy associated plasma protein-A was detectable in all cases but the levels were significantly reduced in second-trimester maternal serum from 18 affected pregnancies. Expressed as multiples of the median (MOM), the results ranged from 0.03 MOM to 0.71 MOM with an overall median value of 0.21 MOM (Mann-Whitney $p<0.001$). From these data it is possible to estimate a probability that any given level of this serum marker is associated with an affected pregnancy. One further sample taken in the first trimester from an affected pregnancy at 11 weeks' gestation had a normal pregnancy associated plasma protein-A level (1.22 MOM). Less markedly reduced levels were found for free beta human chorionic gonadotrophin and inhibin A. We conclude that second-trimester maternal serum pregnancy associated plasma protein-A measurements may be of value as an adjunct to ultrasonography in the prenatal diagnosis of Cornelia de Lange syndrome. A table of likelihood ratios is presented.

L4 ANSWER 23 OF 31 MEDLINE on STN DUPLICATE 17

AN 1999287260 MEDLINE
DN PubMed ID: 10360515
TI Early pregnancy screening for fetal aneuploidy with serum markers and
nuchal translucency.
AU de Graaf I M; Pajkrt E; Bilardo C M; Leschot N J; Cuckle H S; van Lith J M
CS Department of Obstetrics and Gynaecology, Academic Medical Centre,
Amsterdam, The Netherlands.. I.M.deGraaf@AMC.UvA.NL
SO Prenatal diagnosis, (1999 May) 19 (5) 458-62.
Journal code: 8106540. ISSN: 0197-3851.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
ED Entered STN: 19990925
Last Updated on STN: 19990925
Entered Medline: 19990914
AB We determined the aneuploidy detection rate achievable by early pregnancy
screening with pregnancy associated plasma protein (**PAPP**)-**A**, **free** beta human chorionic gonadotrophin (hCG) and
ultrasound nuchal translucency (NT) measurement. Women having prenatal
diagnosis were scanned, and a blood sample was taken and stored. Stored
samples were tested and a total of 37 were found to have Down syndrome, 8
to have Edwards syndrome and 255 were controls. Results were expressed in
multiples of the gestation-specific median (MOM) value in the controls
after regression and, for the serum markers, maternal weight adjustment.
In Down syndrome the medians were for PAPP-A 0.63 MOM (95 per cent
confidence interval (CI) 0.45-0.87); free beta-hCG 1.88 MOM (1.33-2.66);
and NT 2.34 MOM (1.70-3.22). Using these parameters the expected
detection rate for a 5 per cent false-positive rate for different marker
combinations were: 55.3 per cent for PAPP-A and free beta-hCG; 68.4 per
cent for NT alone; and 84.6 per cent for **PAPP-A**, **free** beta-hCG and NT. The median values for Edwards syndrome
were: 0.17 MOM for PAPP-A; 0.18 MOM for free beta-hCG; and 2.64 MOM for
NT. Early pregnancy screening with the combined measurement of maternal
serum PAPP-A and free beta-hCG and fetal nuchal translucency could achieve

a high Down syndrome detection rate.

L4 ANSWER 24 OF 31 MEDLINE on STN DUPLICATE 18
AN 1999171906 MEDLINE
DN PubMed ID: 10073898
TI First-trimester biochemical markers for Down syndrome.
AU Casals E; Aibar C; Martinez J M; Borrell A; Soler A; Ojuel J; Ballesta A
M; Fortuny A
CS Clinical Biochemistry Laboratory, Hospital Clinic, University of Barcelona, Spain.
SO Prenatal diagnosis, (1999 Jan) 19 (1) 8-11.
Journal code: 8106540. ISSN: 0197-3851.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990511
Last Updated on STN: 19990511
Entered Medline: 19990429
AB The value of maternal serum pregnancy-associated protein A (**PAPP-A**), **free** and total beta human chorionic gonadotrophin (fbetahCG, betahCG) and alpha-fetoprotein (AFP) in screening for Down syndrome (DS) in early pregnancy has been assessed. To evaluate the different biochemical markers, 32 DS pregnancies and 267 controls were used for AFP, betahCG and PAPP-A. A subgroup of those (17 DS and 136 controls) were used to evaluate fbetahCG. All analytes were determined in fresh serum samples. Our results give support to the feasibility of maternal serum levels of PAPP-A as the best biochemical marker for DS in the first trimester, and either betahCG or fbetahCG as the second marker. No differences were found between betahCG and fbetahCG distribution levels as expressed as MoMs in normal and DS pregnancies in this study.

L4 ANSWER 25 OF 31 MEDLINE on STN DUPLICATE 19
AN 1998417469 MEDLINE
DN PubMed ID: 9746387
TI First trimester screening for Down's syndrome using maternal serum PAPP-A and free beta-hCG in combination with fetal nuchal translucency thickness.
AU Biagiotti R; Brizzi L; Periti E; d'Agata A; Vanzi E; Cariati E
CS Department of Obstetrics and Gynaecology, University of Florence, Italy.

SO British journal of obstetrics and gynaecology, (1998 Aug) 105 (8) 917-20.
Journal code: 7503752. ISSN: 0306-5456.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199810
ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981026
AB The aim of this study was to evaluate the potential effectiveness of
maternal serum pregnancy-associated plasma protein A (PAPP-A) and free
beta-hCG in combination with nuchal translucency thickness in first
trimester screening for Down's syndrome. Maternal serum levels of PAPP-A
and free beta-hCG were assayed in stored sera from 32 Down's syndrome and
200 unaffected pregnancies. Fetal nuchal translucency was measured by
ultrasound at the time of blood sampling. Screening of Down's syndrome
using a combination of maternal age, **PAPP-A**,
free beta-hCG and nuchal translucency would achieve a detection
rate of 75.8% for a false positive rate of 5%.

L4 ANSWER 26 OF 31 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on
STN
AN 1997:379907 BIOSIS
DN PREV199799679110
TI Trisomy 21 risk evaluation at the first trimester of gestation by ELISA
for **PAPP-a**, **free**-beta-hCG and unconjugated
Estriol in dry blood samples: A prospective study on 805 patients.
AU Schoos, R.; Sgouras, D.; Lesenfant, S.; Verloes, A.; Jamar, M.; Herens,
C.; Girginoudis, P.; Pangalos, C.; Koulischer, L.
CS CHU Liege Centre de Genetique, Campus Sart-Tilman, 4000 Liege, Belgium
SO Cytogenetics and Cell Genetics, (1997) Vol. 77, No. 1-2, pp. 99.
Meeting Info.: 1st European Cytogenetics Conference. Athens, Greece. June
22-25, 1997.
CODEN: CGCGBR. ISSN: 0301-0171.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English

ED Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

L4 ANSWER 27 OF 31 MEDLINE on STN DUPLICATE 20
AN 96330738 MEDLINE
DN PubMed ID: 8735748
TI Trophoblast antigen levels in the first trimester of a trisomy 22 pregnancy.
AU Wheeler D M; Edirisinghe W R; Petchell F; Yovich J L; Murch A R; Saunders D M; Sinosich M J
CS Royal North Shore Hospital, Sydney, NSW, Australia.
SO European journal of obstetrics, gynecology, and reproductive biology, (1996 Jun) 66 (2) 197-9.
Journal code: 0375672. ISSN: 0301-2115.
CY Ireland
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961024
AB We report trophoblast antigen (pregnancy-associated plasma protein-A, **PAPP-A**; **free** beta-human chorionic gonadotrophin, F beta hCG) expression in a trimosy 22 pregnancy. Maternal concentrations of these antigens were depressed prior to detection of abnormalities by ultrasonography. Immunohistochemical findings were consistent with depressed marker expression.

L4 ANSWER 28 OF 31 MEDLINE on STN DUPLICATE 21
AN 90292505 MEDLINE
DN PubMed ID: 1694154
TI Pregnancy-associated plasma protein-A-induced inhibition of human leukocyte elastase: an artifact.
AU Bischof P; Gervaix A; Meisser A; Suter S
CS Departement de Gynecologie et d'Obstetrique, Universite de Geneve, Suisse.
SO Gynecologic and obstetric investigation, (1990) 29 (3) 169-72.
Journal code: 7900587. ISSN: 0378-7346.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199008
ED Entered STN: 19900907

Last Updated on STN: 20000303
Entered Medline: 19900801

AB Pregnancy-associated plasma protein A (PAPP-A), was reported to be an inhibitor in many in vitro systems. Since it was shown that the inhibition of coagulation and complement activity attributed to PAPP-A was in fact due to a contamination by heparin occurring during the purification process, we undertook the present study to see whether the reported PAPP-A-induced inhibition of human leukocyte elastase (HLE) could also be attributed to heparin contamination. PAPP-A was purified from maternal pregnancy EDTA plasma by a method which was previously shown to eliminate contaminating heparin: this preparation was inactive in the HLE assay. But PAPP-A isolated by heparin-Sepharose chromatography, or a **PAPP-A-free** washing of the heparin-Sepharose column were both inhibitors of HLE. Furthermore the inactive PAPP-A preparation, when incubated with the **PAPP-A-free** washing of the heparin-Sepharose column, yielded a high molecular weight preparation which inhibited HLE. It is concluded that PAPP-A is not an inhibitor of HLE and that the inhibition of HLE previously attributed to PAPP-A was due to contaminating heparin.

L4 ANSWER 29 OF 31 MEDLINE on STN DUPLICATE 22
AN 89026983 MEDLINE
DN PubMed ID: 2460147
TI In vitro effects of pregnancy-associated plasma protein-A: artifacts due to heparin.
AU Meisser A; Geinoz A; Bischof P
CS Department of Obstetrics and Gynecology, University of Geneva, Switzerland.
SO Biology of reproduction, (1988 Sep) 39 (2) 373-8.
Journal code: 0207224. ISSN: 0006-3363.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198812
ED Entered STN: 19900308
Last Updated on STN: 19960129
Entered Medline: 19881212

AB Pregnancy-associated plasma protein-A (PAPP-A) has been reported to inhibit elastase activity, lymphoblastogenesis, complement activity, and

thrombin-induced coagulation of fibrinogen. Since some of these results are controversial, we reevaluate here the effects of PAPP-A in these last two systems. By molecular sieve chromatography, PAPP-A immunoreactivity and inhibitory activity on thrombin and complement were dissociated. A **PAPP-A-free** washing of the heparin-Sepharose column used during the purification of PAPP-A showed inhibitory activities similar to those of purified PAPP-A. Furthermore, a preparation of PAPP-A that had not been submitted to heparin-Sepharose chromatography during purification was not active in either assays. Thus, the anticoagulant and anti-complement effects previously attributed to PAPP-A were due to a contaminant of low molecular mass. We believe that this contaminant is probably heparin. A protocol to eliminate free and PAPP-A-bound heparin is presented herein, and implications for other previously reported in vitro effects of PAPP-A are discussed.

L4 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1984:421791 CAPLUS
DN 101:21791
TI Pregnancy-associated plasma protein-A (PAPP-A) is a specific inhibitor of the third component of human complement
AU Bischof, Paul; Geinoz, Antoine
CS Dep. Obstetr. Gynecol., Univ. Geneva, Geneva, 1211/4, Switz.
SO Trophoblast Research (1984), 1(Fetal Nutr., Metab., Immunol.), 323-33
CODEN: TRREEN; ISSN: 0891-9925
DT Journal
LA English
AB PAPP-A is a macromol. glycoprotein associated with pregnancy, which inhibits complement-induced hemolysis and reversibly binds heparin. Because of the inhibitory effect of heparin on the complement cascade, it was not clear if the inhibition of complement activity observed with PAPP-A (isolated from heparin plasma) was attributable to the heparin moiety bound to PAPP-A. It was determined that heparin exerts an inhibitory effect on complement

activity, but that heparin-**free PAPP-A** is also inhibitory. PAPP-A specifically inhibits complement C3 by directly binding to it and not by inhibiting C3 convertase.

L4 ANSWER 31 OF 31 MEDLINE on STN DUPLICATE 23
AN 84221805 MEDLINE
DN PubMed ID: 6203109
TI Pregnancy-associated plasma protein A (PAPP-A) specifically inhibits the third component of human complement (C3).
AU Bischof P; Geinoz A; Herrmann W L; Sizonenko P C
SO Placenta, (1984 Jan-Feb) 5 (1) 1-7.
Journal code: 8006349. ISSN: 0143-4004.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198407
ED Entered STN: 19900320
Last Updated on STN: 20021030
Entered Medline: 19840711
AB Pregnancy-associated plasma protein A (PAPP-A), a macromolecular glycoprotein associated with pregnancy, was shown to inhibit complement-induced haemolysis and to bind heparin reversibly. Because of the inhibitory effects of heparin on the complement cascade it was not clear if the inhibition of complement activity observed with PAPP-A (isolated from heparin plasma) was attributable to the heparin moiety bound to PAPP-A. This work demonstrates that heparin exerts an inhibitory effect on complement activity but that heparin-**free PAPP -A** is also inhibitory. PAPP-A specifically inhibits C3 by binding to this complement subcomponent and not by inhibiting C3 convertase as demonstrated for C3 inactivator.